

CLAIMS

1. A strain of a micro-organism characterized in that one or more of its NADPH-oxidizing activities have been limited.

5 2. A strain according to Claim 1 characterized in that one or more of its NADPH-oxidizing activities have been limited by the deletion of one or more genes coding for a quinone oxidoreductase and/or a soluble transhydrogenase.

3. A strain according to either of Claims 1 and 2 characterized in that it has also undergone modifications that favour one or more of its NADP⁺-reducing enzyme activities.

10 4. A strain according to Claim 3 characterized in that it has undergone the deletion of one or more genes coding for a phosphoglucose isomerase and/or a phosphofructokinase.

5. A strain according to any of Claims 1 to 4 characterized in that it has also undergone the modification of one or more genes coding for a dihydrolipoamide
15 dehydrogenase and/or a glyceraldehyde 3-phosphate dehydrogenase so as to cause it to utilize NADP preferentially.

6. A strain according to any of Claims 1 to 5 characterized in that it also overexpresses one or more genes coding for a glucose 6-phosphate dehydrogenase, or a 6-phosphogluconolactonase, or a 6-phosphogluconate dehydrogenase, or an isocitrate
20 dehydrogenase or a membrane-bound transhydrogenase.

7. A strain according to any of Claims 1 to 6 characterized in that it has also undergone the deletion of one or more genes coding for a 6-phosphogluconate dehydratase, or a malate synthase, or an isocitrate lyase or an isocitrate dehydrogenase kinase/phosphatase.

8. A strain according to any of Claims 1 to 7, characterized in that it comprises
25 one or more endogenous or exogenous genes coding for enzymes involved in the biotransformation of a substance of interest.

9. A strain according to any of Claims 1 to 8, characterized in that it comprises one or more selection marker genes.

10. A strain according to any of Claims 1 to 9 characterized in that it is selected
30 among the following: *Aspergillus sp.*, *Bacillus sp.*, *Brevibacterium sp.*, *Clostridium sp.*,

Corynebacterium sp., *Escherichia sp.*, *Gluconobacter sp.*, *Penicillium sp.*, *Pichia sp.*, *Pseudomonas sp.*, *Rhodococcus sp.*, *Saccharomyces sp.*, *Streptomyces sp.*, *Xanthomonas sp.* or *Candida sp.*

11. A method for the preparation of strains optimized according to any of Claims 1
5 to 10 characterized in that it involves the deletion of one or more genes coding for a quinone
oxidoreductase and/or a soluble transhydrogenase, and if required the deletion of one or more
genes coding for a phosphoglucose isomerase, or a phosphofructokinase, or a 6-
phosphogluconate dehydratase, or a malate synthase, or an isocitrate lyase or an isocitrate
dehydrogenase kinase/phosphatase, and/or the modification of one or more genes coding for a
10 dihydrolipoamide dehydrogenase and/or a glyceraldehyde 3-phosphate dehydrogenase, so as
to cause it to utilize NADP preferentially, which deletions and modifications are carried out by
appropriate means, and/or the overexpression of one or more genes coding for a glucose 6-
phosphate dehydrogenase, or a 6-phosphogluconolactonase, or a 6-phosphogluconate
dehydrogenase, or an isocitrate dehydrogenase or a membrane transhydrogenase, either by
15 converting the strain by means of an appropriate vector containing one or more genes coding
for one or more enzymes involved in the biotransformation of a substance of interest and/or
one or more selection marker genes, or by modifying the strength of the endogenous promoter
or promoters controlling the gene or genes to be overexpressed.

12. A method for the production of a substance of interest formed by a biosynthesis
20 route of which at least one step is NADPH-dependent characterized in that it comprises the
following two steps:

- a) Growth in culture of micro-organisms optimized according to any of Claims 1 to 10 in
an appropriate culture medium that favours their growth and contains substances
necessary for carrying out biotransformations by fermentation or bioconversion, except
25 NADPH.
- b) Extraction of the substance of interest from the medium and if necessary its
purification.

13. A method according to Claim 12 characterized in that the substance of interest is an
amino acid, or a vitamin, or a sterol, or a flavonoid, or a fatty acid, or an organic acid, or a
30 polyol or a hydroxyester.